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ABSTRACT

This fact sheet uses a question-and-answer format to summarize what is known about the genetic causes of mental retardation. Questions and answers address the following topics: what genetics is; how a person's genes can cause mental retardation; how often mental retardation is inherited (up to 60 percent of severe mental retardation has genetic causes); causes of genetic disorders (chromosomal disorders, single-gene disorders, and multifactorial disorders); how genetic disorders are inherited (dominant inheritance, recessive inheritance, and X-linked or sex-linked inheritance); and the possibilities of using gene therapy to treat genetic disorders causing mental retardation. (Contains 10 references.) (DB)

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ARC Q&A #101-50

The Arc
A national organization on mental retardation

S. A. Davis

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Q&A

Genetic Causes of Mental Retardation

What is genetics?

Genetics is "the science that studies the principles and mechanics of heredity, or the means by which traits are passed from parents to offspring" (Glanze, 1996). Through genetics a number of specific disorders have been identified as being genetically caused. One example is fragile X syndrome, a common genetic cause of mental retardation, which is caused by the presence of a single non-working gene (called the FMR-1 gene) on a child's X chromosome.

Genetics originated in the mid-19th century when Gregor Mendel discovered over a ten year period of experimenting with pea plants that certain traits are inherited. His discoveries provided the foundation for the science of genetics. Mendel's findings continue to spur the work and hopes of scientists to uncover the mystery behind how our genes work and what they can reveal to us about the possibility of having certain diseases and conditions. The scientific field of genetics can help families affected by genetic disorders to have a better understanding about heredity, what causes various genetic disorders to occur, and what possible prevention strategies can be used to decrease the incidence of genetic disorders.

Can a person's genes cause mental retardation?

Some genetic disorders are associated with mental retardation, chronic health problems and developmental delay. Because of the complexity of the human body, there are no easy answers to the question of what causes mental retardation. Mental retardation is attributable to any condition that impairs development of the brain before birth, during birth or in the childhood years (The Arc, 1993). As many as 50 percent of people with mental retardation have been found to possess more than one causal factor (AAMR, 1992). Some research has determined that in 75 percent of children with mild mental retardation the cause is unknown (Kozma & Stock, 1993).

The field of genetics has important implications for people with mental retardation. Over 350 inborn errors of metabolism have been identified, most of which lead to mental retardation (Scriver, 1995). Yet, the possibility of being born with mental retardation or developing the condition later in life can be caused by multiple factors unrelated to our genetic make-up. It is caused not only by the genotype (or genetic make-up) of the individual, but also by the possible influences of environmental factors. Those factors can range from drug use or nutritional deficiencies to poverty and cultural deprivation.

How often is mental retardation inherited?

Since the brain is such a complex organ, there are a number of genes involved in its development. Consequently, there are a number of genetic causes of mental retardation. Most identifiable causes of severe mental retardation (defined as an IQ of 50 or less) originate from genetic disorders. Up to 60 percent of severe mental retardation can be attributed to genetic causes making it the most common cause in cases of severe mental retardation (Moser, 1995). People with mild mental retardation (defined as an IQ between 50 and 70-75) are not as likely to inherit mental retardation due to their genetic make-up as are people with severe mental retardation. People with mild mental retardation are more likely to have the condition due to environmental factors, such as nutritional state, personal health habits, socioeconomic level, access to health care and exposure to pollutants and chemicals, rather than acquiring the condition genetically (Nelson-Anderson & Waters, 1995). Two of the most common genetically transmitted forms of mental retardation include Down syndrome (a chromosomal disorder) and fragile X syndrome (a single-gene disorder).

What causes genetic disorders?

Over 7,000 genetic disorders have been identified and catalogued, with up to five new disorders being discovered every year (McKusick, 1994). Genetic disorders are typically broken down into three types: Chromosomal, single-gene and multifactorial.

Chromosomal disorders affect approximately 7 out of every 1,000 infants. The disorder results when a person has too many or too few chromosomes, or when there is a change in the structure of a chromosome. Half of all first-trimester miscarriages or spontaneous abortions occur as a result of a chromosome abnormality. If the child is born, he or she usually has multiple birth defects and mental retardation.

Most chromosomal disorders happen sporadically. They are not necessarily inherited (even though they are considered to be genetic disorders). In order for a genetic condition to be inherited, the disease-causing gene must be present within one of the parent's genetic code. In most chromosomal disorders, each of the parent's genes are normal. However, during cell division an error in separation, recombination or distribution of chromosomes occurs. Examples of chromosomal disorders include Down syndrome, Trisomy 13, Trisomy 18 and Cri du chat.

Single-gene disorders (sometimes called inborn errors of metabolism or Mendelian disorders) are caused by non-working genes. Disorders of metabolism occur when cells are unable to produce proteins or enzymes needed to change certain chemicals into others, or to carry substances from one place to another. The cell's inability to carry out these vital internal functions often results in mental retardation. Approximately 1 in 5,000 children are born with defective enzymes resulting in inborn errors of metabolism (Batshaw, 1992). Although many conditions are generally referred to as "genetic disorders," single-gene disorders are the most easy to identify as true genetic disorders since they are caused by a mutation (or a change) within a single gene or gene pair.

Combinations of multiple gene and environmental factors leading to mental retardation are called **multifactorial disorders**. They are inherited but do not share the same inheritance patterns typically found in single-gene disorders. It is unclear exactly why they occur. Their

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inheritance patterns are usually much more complex than those of single gene disorders because their existence depends on the simultaneous presence of heredity and environmental factors. For example, weight and intelligence are traits inherited in this way (Batshaw, 1992). Other common disorders, including cancer and hypertension, are examples of health problems caused by the environment and heredity. Multifactorial disorders are very common and cause a majority of birth defects. Examples of multifactorial disorders include heart disease, diabetes, spina bifida, anencephaly, cleft lip and cleft palate, clubfoot and congenital heart defects.

How are genetic disorders inherited?

Genetic disorders can be inherited in much the same way a person can inherit other characteristics such as eye and hair color, height and intelligence. Children inherit genetic or hereditary information by obtaining genes from each parent. There are three common types or modes of inheritance: dominant, recessive and X-linked (or sex-linked).

Dominant inheritance occurs when one parent has a dominant, disease-causing gene which causes abnormalities even if coupled with a healthy gene from the other parent. Dominant inheritance means that each child has a 50 percent chance of inheriting the disease-causing gene. An example of dominant inheritance associated with mental retardation is tuberous sclerosis.

Recessive inheritance occurs when both parents carry a disease-causing gene but outwardly show no signs of disease. Parents of children with recessive conditions are called "carriers" since each parent carries one copy of a disease gene. They show no symptoms of having a disease gene and remain unaware of having the gene until having an affected child. When parents who are carriers give birth, each child has a 25 percent chance of inheriting both disease genes and being affected. Each child also has a 25 percent chance of inheriting two healthy genes and not being affected, and a 50 percent chance of being a carrier of the disorder, like their parents. Examples of disorders which are inherited recessively and are also associated with mental retardation include phenylketonuria (PKU) and galactosemia.

X-linked or sex-linked inheritance affects those genes located on the X chromosome and can be either X-linked recessive or X-linked dominant. The X-linked recessive disorder, which is much more common compared to X-linked dominant inheritance, is referred to as a sex-linked disorder since it involves genes located on the X chromosome. It occurs when an unaffected mother carries a disease-causing gene on at least one of her X chromosomes. Since females have two X chromosomes, they are usually unaffected carriers because the X chromosome that does not have the disease-causing gene compensates for the X chromosome that does. Therefore, they are less likely than males to show any symptoms of the disorder unless both X chromosomes have the disease-causing gene.

If a mother has a female child, the child has a 50 percent chance to inherit the disease gene and be a carrier and pass the disease gene on to her sons (March of Dimes, 1995). On the other hand, if a mother has a male child, he has a 50 percent chance of inheriting the disease-causing gene since he has only one X chromosome. Consequently, males cannot be carriers of X-linked recessive disorders. If a male inherits an X-linked recessive disorder, he is affected. Some examples of X-linked inheritance associated with mental retardation include fragile X syndrome, Hunter syndrome, Lesch Nyhan syndrome and Duchenne muscular dystrophy.

Can genetic disorders which cause mental retardation be fixed?

In the past, only a few genetic disorders could be detected and treated early enough to prevent disease. However, the Human Genome Project, an international project among scientists to identify all the 60,000 to 100,000 genes within the human body, is significantly increasing our ability to discover more effective therapies and prevent inherited disease (National Center for Human Genome Research, 1995). As more disease-causing genes are identified, scientists can begin developing genetic therapies to alter or replace a defective gene. However, the development of gene therapies is still in the infancy stage.

Gene therapy (also called somatic-cell gene therapy) is a procedure in which "healthy genes" are inserted into individuals to cure or treat an inherited disease or illness. Although there is a role for gene therapy in the prevention of mental retardation, it will most likely benefit only those people who have single-gene disorders, such as Lesch-Nyhan disease, Gaucher disease and phenylketonuria (PKU) that cause severe mental retardation (Moser, 1995). Gene therapy is far less likely to provide treatment of mild mental retardation which accounts for 87 percent of all cases of mental retardation (The Arc, 1993).

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